REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at 858 720 5133.

Status of the Claims

Pending claims

Claims 1 to 23, 40, 41, 67 to 85 and 93 to 108 are pending (claims 24 to 39, 42 to 66 and 86 to 92, were canceled, without prejudice, in Applicants' last response).

The Restriction Requirement and Election

The Patent Office alleged that the pending claims of the application are directed to nine separate and distinct inventions under 35 U.S.C. §121, and requested an election of a sequence of SEQ ID NOs:19-54 for each of Groups I to IX.

In response to the restriction requirement, Applicants elected, with traverse, Group I, claims 1-23, 40, 41, 67- 81, and 82-85, as pertaining to SEQ ID NO:21 and SEQ ID NO:30, drawn to isolated nucleic acids encoding a polypeptide having phosphatase activity, methods of expressing said nucleic acids, and oligonucleotide probes.

In their traversal to the restriction requirement Applicants requested that the Patent Office reconsider and join (nucleic acid/amino acid sequences) SEQ ID NOS:21, 30; 22, 31; 23, 32; 26, 35; and 45, 46 for Group I. Applicants set forth distinct and specific errors in the restriction requirement and reasons for the Patent Office to reconsider and withdraw, in part, the restriction requirement. Accordingly, Applicants have preserved their right to petition the restriction to the Group Director under 37 CFR §1.144; see also MPEP §818.03(c); pg 800-60, 8th Edition, August 2001.

Outstanding Rejections

Claims 3 to 5, 67 to 84 and 93 to 108 are rejected under 35 U.S.C. §112, second paragraph. The rejection of claims 3 to 5, 6 to 14, 16 to 21, 22, 23, 41, 67 to 81 and 82 to 85 is maintained and claims 93 to 108 are newly rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention. The rejection of claims 3 to 5, 6 to 14, 16 to 21, 22, 23, 40, 41, 67 to 81 and 82 to 85 is maintained and claims 93 to 108 are newly rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the Claim Amendments

Support for the claim amendments can be found throughout the specification. For example, support for claimed directed to nucleic acids defined by, inter alia, their ability to hybridize to an exemplary nucleic acid under various hybridization conditions can be found, inter alia, in paragraphs 168 to 179, pages 40 to 42, of the specification. Accordingly, Applicants respectfully submit that no new matter is introduced by the instant amendments.

Issues under 35 U.S.C. §112, second paragraph

Claims 3 to 5, 67 to 84 and 93 to 108 are rejected under 35 U.S.C. §112, second paragraph, for reasons set forth on line 10, page 2, to line 5, page 4. The instant amendment addresses these issues.

Issues under 35 U.S.C. §112, first paragraph

Written Description

The rejection of claims 3 to 5, 6 to 14, 16 to 21, 22, 23, 41, 67 to 81 and 82 to 85 is maintained and claims 93 to 108 are newly rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention.

Applicants thank the Examiner for withdrawing the §112, first paragraph, written description rejection of claims 15 and 40.

However, the Patent Office remains concerned that some of the claims rejected under §112, first paragraph, for lack of written description do not have a functional limitation. This instant amendment addresses this issue. For example:

Amended claims 3 to 5 are directed to nucleic acids at least 20 residues in length that hybridize to a nucleic acid encoding a polypeptide having phosphatase activity, or its complementary sequence, under specific conditions.

Amended claims 6 to 13 are directed to nucleic acids having a specific sequence identity to a nucleic acid encoding a polypeptide having phosphatase activity and a sequence as set forth in SEQ ID NO:30.

Amended claim 14 is directed to nucleic acids encoding a polypeptide having phosphatase activity and a sequence as set forth in SEQ ID NO:30 comprising at least one conservative amino acid substitution.

Amended claim 16 is directed to nucleic acids encoding a polypeptide having phosphatase activity and comprising at least 20 consecutive bases of a sequence as set forth in SEQ ID NO:21, and sequences complementary thereto.

Amended claims 17 to 21 directed to nucleic acids encoding a polypeptide having phosphatase activity and having a sequence identity to at least 20 consecutive bases of a sequence as set forth in SEQ ID NO:21 as determined by analysis with a specific sequence comparison algorithm.

Amended claim 22 is directed to nucleic acids encoding a polypeptide having phosphatase activity having a sequence as set forth in SEQ ID NO:30. Amended claim 23 is directed to nucleic acids encoding a polypeptide having phosphatase activity comprising at least 20 consecutive amino acids of a polypeptide having a sequence as set forth in SEQ ID NO:30.

Amended claim 40 is directed to methods of producing a polypeptide having phosphatase activity and a sequence as set forth in SEQ ID NO:30, or a sequence encoded by a nucleic acid as set forth in claim 1, comprising introducing the nucleic acid into a host cell under conditions that allow expression of the polypeptide.

Amended claim 41 is directed to methods producing a polypeptide having phosphatase activity comprising at least 10 amino acids of a sequence as set forth in SEQ ID NO:30, or a polypeptide having phosphatase activity encoded by a nucleic acid as set forth in claim 1, comprising introducing the nucleic acid encoding the polypeptide, operably linked to a promoter, into a host cell under conditions that allow expression of the polypeptide.

Amended claim 67 is directed to nucleic acid probes for identifying or isolating a nucleic acid encoding a polypeptide having phosphatase activity comprising an oligonucleotide from about 10 to 50 nucleotides in length and having an area of at least 10 contiguous nucleotides that have a sequence identity to a nucleic acid target region comprising a nucleic acid sequence as set forth in SEQ ID NO:21, or its complementary sequence, and which hybridizes to the nucleic acid target region to form a detectable target:probe duplex under specific hybridization conditions.

Amended claim 82 is directed to nucleic acid probes for identifying or isolating a nucleic acid encoding a polypeptide having phosphatase activity comprising an oligonucleotide from about 15 to 50 nucleotides in length and having an area of at least about 20 contiguous nucleotides having a sequence identity to a nucleic acid target region of the nucleic acid sequence as set forth in SEQ ID NO:21, and which hybridizes to the nucleic acid target region under specific hybridization conditions.

Amended claim 83 is directed to nucleic acid probes for identifying or isolating a nucleic acid encoding a polypeptide having phosphatase activity comprising an oligonucleotide from about 15 to 50 nucleotides in length and having an area of at least about 20 contiguous nucleotides having a sequence identity to a nucleic acid target region of the nucleic acid sequence as set forth in SEQ ID NO:21, and which hybridizes to the nucleic acid target region under specific hybridization conditions.

Amended claim 84 is directed to nucleic acid probes for identifying or isolating a nucleic acid encoding a polypeptide having phosphatase activity comprising an oligonucleotide from about 15 to 50 nucleotides in length and having an area of at least about 20 contiguous nucleotides having a sequence identity to a nucleic acid target region of the nucleic acid sequence as set forth in SEQ ID NO:21, and which hybridizes to the nucleic acid target region under specific hybridization conditions.

Amended claim 85 is directed to nucleic acid probes for isolation or identification of phosphatase genes having a sequence which is the same as or fully complementary to a sequence as set forth in SEQ ID NO:21.

Because all of the pending, amended claims are clearly associated with a functional limitation, Applicants respectfully aver that the USPTO guidelines recognizing that

the written description requirement is met for a genus of polynucleotides described by structure (e.g., an exemplary sequence), a physico-chemical property (e.g., a % sequence identity or stringent hybridization) and a defined function, do apply.

As noted in the attached expert declaration by Dr. Jay Short, who was an expert in the field of molecular biology and enzyme development at the time of the invention, procedures for identifying nucleic acids that encode enzymes such as phosphatases were conventional and routine in the art at the time of the invention. Dr. Short declares that procedures for identifying polypeptides having phosphatase activity were conventional and routine in the art at the time of the invention. For example, an exemplary assay for identifying polypeptides having phosphatase activity is described in the paragraph spanning pages 39 and 40 of priority document PCT/US97/10784, published as WO 97/48416, which is expressly incorporated by reference. Dr. Short declares that one of ordinary skill in the art using the teaching of the specification could have made and expressed nucleic acids having a percent sequence identity to an exemplary nucleic acid, or, which hybridized under defined conditions to an exemplary nucleic acid, and using routine screening could have determined with predicable positive results which of those nucleic acids encoded a polypeptide having phosphatase activity, or, which of those nucleic acids identified a phosphatase encoding sequence. Thus, using the teaching of the specification one of ordinary skill in the art would have been able to ascertain the scope of the claimed genus of phosphatase-encoding and phosphatase-identifying nucleic acids with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing. Accordingly, based on the USPTO guidelines (see, e.g., Example 14 of the guidelines, copy attached herein) for the written description requirement, the pending, amended claims comply with the requirements of section 112, first paragraph.

The Patent Office correctly notes that hybridization to a nucleic acid that encodes a phosphatase does not necessitate that the claimed hybridizing nucleic acid (e.g., a probe) itself encodes a phosphatase. However, it is alleged that because claimed hybridizing nucleic acids (e.g., probes) do not themselves encode a phosphatase, these claims are not sufficiently described by the specification to satisfy the written description requirement.

However, Applicants respectfully aver that the claimed genus of nucleic acids only needs to be sufficiently correlated to a particular, known structure (e.g., an exemplary

sequence encoding a phosphatase) to be sufficiently described by the specification to satisfy the written description requirement. The Federal Circuit stated:

> More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the functions of claimed genus of nucleic acids (e.g., as phosphatase-encoding or phosphatase-identifying nucleic acids) is sufficiently correlated to a particular, known structure (e.g., the exemplary sequences) and a physical (physico-chemical) property (e.g., percent sequence identity or stringent hybridization) to satisfy the written description requirement (also, please note discussion, above, regarding the instant amendment to the claims). Accordingly, the sequences of the invention are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Accordingly, Applicants respectfully submit that the pending, amended claims meet the written description requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are sufficiently described in the specification to overcome the rejection based upon the written description requirement of 35 U.S.C. §112, first paragraph.

It is noted in the office action that Exhibit A from Applicants' response of July 25, 2003, was not matched with the file. To ensure the instant record is complete, another copy of Exhibit A from Applicants' last response is attached herein.

Enablement

The rejection of claims 3 to 5, 6 to 14, 16 to 21, 22, 23, 40, 41, 67 to 81 and 82 to 85 is maintained and claims 93 to 108 are newly rejected under 35 U.S.C. §112, first paragraph,

as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. It is alleged that it would require undue experimentation for one skilled in the art to arrive at the genus of claimed nucleic acids.

The Patent Office states that the specification is enabling for an isolated nucleic acid encoding a polypeptide having phosphatase activity, wherein said polypeptide comprises SEQ ID NO:30. However, it is alleged, inter alia, that the specification does not reasonable provide enablement for any nucleic acid or polynucleotide probe which is fully complementary to a portion of SEQ ID NO:21.

The Patent Office remains concerned that some of the claims rejected under §112, first paragraph, for lack of written description do not have a functional limitation. The instant amendment addresses this issue, as discussed above.

The Patent Office is also concerned that a genus of nucleic acids comprising at least 50% sequence identity to the exemplary nucleic acid is so large it might take undue experimentation to make such a genus. The instant amendment addresses this issue; for example, amended claim 1 is now directed to nucleic acids comprising sequences having at least 70% sequence identity to SEQ ID NO:21, and encoding a polypeptide having a phosphatase activity, and their complementary sequences.

In discussing its concerns regarding enablement for the claimed genus of nucleic acids having at least 50% sequence identity to SEQ ID NO:21, the Patent Office alleged that the specification does not enable this genus because (A) regions of the polynucleotide structure which may be modified without its functional activity; (B) the general tolerance of the claimed polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue of the polynucleotide with an expectation of obtaining the desired biological function; and, (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Applicants respectfully aver that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, the genus of phosphatase-encoding and phosphatase-identifying (e.g., probes) nucleic acids of the claimed invention. In support, Applicants submit for consideration a Rule 132 declaration by Dr. Jay Short, who was an expert in the field of molecular biology and enzyme development at the time of the invention.

Dr. Short declares that procedures for modifying and expressing nucleic acids were conventional and routine in the art at the time of the invention. Dr. Short declares that procedures for determining the activity of the expressed modified nucleic acids and determining if the nucleic acids expressed a polypeptide with phosphatase activity were conventional and routine in the art at the time of the invention. Dr. Short declares that procedures for determining sequence identity to an exemplary nucleic acid or whether a nucleic acid hybridized to a target nucleic acid under defined conditions were routine in the art at the time of the invention. Dr. Short declares that procedures for expressing and screening for phosphatase activity were conventional and routine in the art at the time of the invention.

Dr. Short declares that one of ordinary skill in the art using the teaching of the specification would have been able to make and use the genus of compositions of the invention, including a genus of phosphatase-encoding or phosphatase-identifying nucleic acids having at least 70% sequence identity to the exemplary nucleic acid, or phosphatase-encoding or phosphatase-identifying nucleic acids that hybridize under defined hybridization conditions to the exemplary nucleic acid, without undue experimentation. It was considered routine by one skilled in the art at the time of the invention to screen for multiple substitutions or modifications of a nucleic acid or a polypeptide for functional variations, including screening for a genus of phosphatase-encoding nucleic acids or a genus of phosphatases. It was considered routine by one skilled in the art at the time of the invention to screen for subsequences of nucleic acids that can identify or encode phosphatases or enzymatically active fragments. It was considered routine by one skilled in the art at the time of the invention to screen for subsequences of nucleic acids that can identify by hybridization a phosphatase-encoding nucleic acid. For example, high through-put methods for screening for enzyme activity, such as phosphatase activity, were well known in the art. While the numbers of samples needed to be screened may have been high, the screening procedures were routine and successful results (e.g., finding a genus of nucleic acids encoding phosphatases) predictable. At the time of the invention it would have been considered routine by one skilled in the art to generate and screen multiple substitutions or multiple modifications in an exemplary nucleic acid sequence and predictably generate a genus of phosphatase-encoding nucleic acids or a genus of phosphatases.

Dr. Short declares that it would not have been necessary for the skilled artisan to understand which regions of the phosphatase-encoding or phosphatase-identifying nucleic acid or phosphatase structure could be modified without loss of functional activity. Dr. Short declares that it would not have been necessary for the skilled artisan to understand which specific regions of phosphatase sequence or structure needed to be modified without affecting function or activity to routinely generate the claimed genus of phosphatase-encoding or phosphatase-identifying nucleic acids. Dr. Short declares that methods for sequence modifications were sufficiently comprehensive, routine and predictable at the time of the invention to predictably generate phosphatase-encoding or phosphatase-identifying sequences without need of knowing which specific regions of phosphatase sequence or structure affected phosphatase function or activity. Methods known at the time of the invention for modifying nucleic acid sequences in combination with high through-put enzyme activity screening known at the time of the invention, made methods that require previous knowledge of protein structure, including secondary or tertiary structure, active site sequences, and the like obsolete and unnecessary. Dr. Short declares that at the time of the invention, high through-put *in vivo* (e.g., whole cell) nucleic acid expression and enzyme activity screening protocols were well known in the art. Dr. Short declares that the specification sets forth an exemplary phosphatase screening assay to determine if a nucleic acid or polypeptide is within the scope of the claimed genus, inter alia, in the paragraph spanning pages 39 and 40 of the WO 97/48416 specification. Dr. Short declares that using methods known in the art at the time of the invention it would not have been necessary to understand which specific regions of phosphatase structure needed to be modified to generate a genus of nucleic acids or polypeptides for practicing the invention without undue experimentation. Dr. Short declares that the specification presented to the skilled artisan a rational and predictable scheme for making the genus of phosphatase-encoding and phosphatase-identifying sequences, including a rational and predictable scheme for modifying any nucleic acid residue of the exemplary nucleic acid with an expectation of obtaining the desired function. Dr. Short declares that the specification provided sufficient guidance to one of ordinary skill in the art to make and use the claimed genus of nucleic acids or polypeptides to practice the invention.

Applicants respectfully submit that the pending claims meet the enablement requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants

respectfully submit that the specification sufficiently described how to make and use the claimed methods to satisfy the requirements of 35 U.S.C. §112, first paragraph.

CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs. Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952. Please credit any overpayment to this account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at 858 720 5133.

Respectfully submitted,

Date: June 04, 2004

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